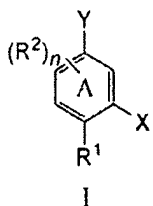


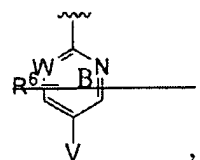
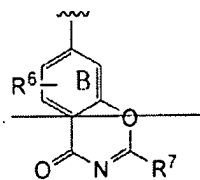
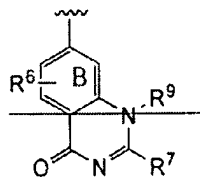
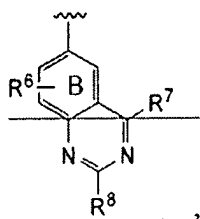
## AMENDMENTS TO THE CLAIMS

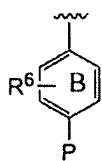
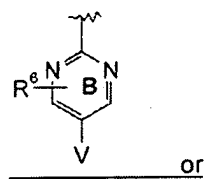
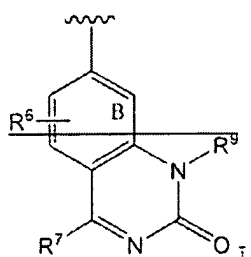
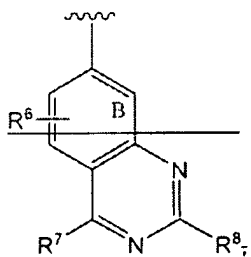
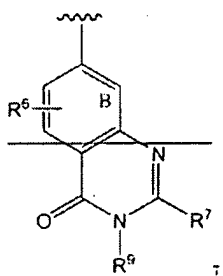
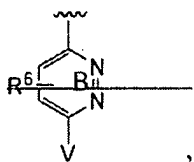
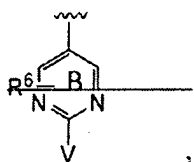
This listing of the claims will replace all prior versions of the claims and listing of the claims in the application:

1. (Currently Amended) A compound having formula (I):



or a pharmaceutically acceptable derivative thereof, wherein X is





;

R<sup>1</sup> is selected from halogen, hydroxyl, lower alkyl, lower cycloalkyl, alkynyl, trifluoromethyl, methoxy, trifluoromethoxy, cyano, -NH<sub>2</sub>, -NR<sup>4</sup>R<sup>5</sup> and -OR<sup>4</sup>;

R<sup>2</sup> is attached to any available carbon atom of the phenyl ring A and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NMe<sub>2</sub>, -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>;

n is 0 or 1;

Y is -L-R<sup>3</sup> or R<sup>11</sup>;

R<sup>3</sup> is selected from hydrogen, alkyl, -OR<sup>4</sup>, substituted alkyl, cycloalkyl, -CR<sup>4</sup>cycloalkyl, heteroaryl, substituted heteroaryl, heterocycle and substituted heterocycle;

L is -C(=O)NH-, -NH(C=O)-, -SO<sub>2</sub>NH-, -NHSO<sub>2</sub>-, or -C(=O)-;

R<sup>11</sup> is an optionally substituted 5-membered heteroaryl;

~~W is CH or N;~~

V is -M-R<sup>10</sup> or R<sup>14</sup>;

M is -C(=O)NR<sup>4</sup>-, -NR<sup>4</sup>(C=O)-, -NR<sup>4</sup>(C=O)NR<sup>4</sup>-, -NR<sup>4</sup>SO<sub>2</sub>-, or -C(=O)-;

R<sup>14</sup> is aryl or heteroaryl optionally substituted with up to three R<sup>12</sup>;

P is -Q-R<sup>10</sup> or R<sup>15</sup>;

Q is -NR<sup>4</sup>(C=O)-, -NR<sup>4</sup>(C=O)NR<sup>4</sup>-, -SO<sub>2</sub>NR<sup>4</sup>-, -NR<sup>4</sup>SO<sub>2</sub>-, or -C(=O)-;

R<sup>15</sup> is aryl or heteroaryl optionally substituted with up to three R<sup>12</sup>;

R<sup>4</sup> and R<sup>5</sup> are each selected independently from hydrogen, lower alkyl and lower cycloalkyl;

R<sup>6</sup> is attached to any available carbon atom of the phenyl ring B and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NH<sub>2</sub>, -NMe<sub>2</sub>, -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, -NHC(=O)R<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>;

~~R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen, alkyl, substituted alkyl, aryl, and cycloalkyl;~~

~~R<sup>9</sup> is hydrogen, alkyl, substituted alkyl or cycloalkyl;~~

R<sup>10</sup> is alkyl, substituted alkyl, aryl, or -(CH<sub>2</sub>)<sub>t</sub>D-(CH<sub>2</sub>)<sub>e</sub>-R<sup>13</sup>;

t is selected from 0, 1, 2 and 3; e is selected from 0, 1, 2 and 3;

D is selected from a bond, an optionally substituted heterocycle, an optionally substituted aryl, -O-, -S-, -C(=O)-, -NR<sup>4</sup>(C=O)-, -C(=O)NR<sup>4</sup>-, -S(O)-, SO<sub>2</sub>NR<sup>4</sup>-, SO<sub>2</sub>-, and -NR<sup>4</sup>-;

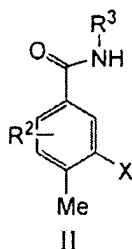
R<sup>12</sup> is selected from R<sup>10</sup>, NO<sub>2</sub>, CN, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NMe<sub>2</sub>, -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -

NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>; and

R<sup>13</sup> is selected from an optionally substituted five- to seven-membered heterocyclic ring, an optionally substituted five- to seven-membered heteroaryl ring and an optionally substituted fused bicyclic ring,

with the proviso that when Q is CO then Y is not oxadiazolyl and L is not -C(=O)NH- or -NHC(=O).

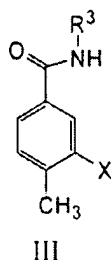
2. (Original) The compound of claim 1, having formula (II):



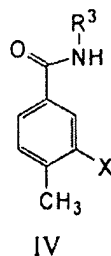
where R<sup>2</sup> is selected from hydrogen, methyl and halogen; and

R<sup>3</sup> is selected from alkyl, -OR<sup>4</sup>, substituted alkyl, cycloalkyl, heteroaryl and substituted heteroaryl.

3. (Previously Presented) The compound of claim 1 having formula (III):

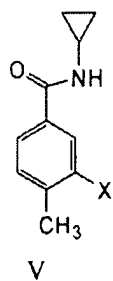


4. (Previously Presented) The compound of claim 1 having formula (IV):

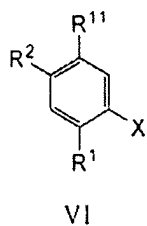


wherein R<sup>3</sup> is selected from lower alkyl, lower cycloalkyl, heteroaryl, and substituted heteroaryl.

5. (Previously Presented) The compound of any of claim 1 having formula (V):

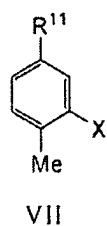


6. (Original) The compound of claim 1 having formula (VI):

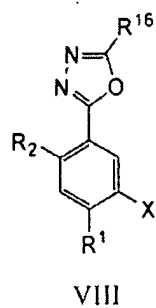


where R<sup>1</sup> is selected from methyl, cyclopropyl and halogen; and  
R<sup>2</sup> is selected from hydrogen, methyl and halogen.

7. (Previously Presented) The compound of claim 1 having formula (VII):



8. (Previously Presented) The compound of claim 1 having formula (VIII):



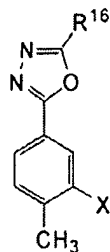
wherein

R<sup>1</sup> is selected from methyl, cyclopropyl and halogen;

R<sup>2</sup> is selected from hydrogen, methyl and halogen; and

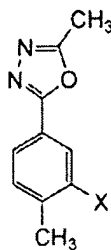
R<sup>16</sup> is selected from hydrogen, lower alkyl and lower cycloalkyl.

9. (Previously Presented) The compound of claim 1 having formula (IX):



IX

10. (Previously Presented) The compound of claim 1 having formula:



11. (Cancelled)

12. (Previously Presented) The compound of claim 1, wherein R<sup>6</sup> is lower alkyl or hydrogen.

13. (Previously Presented) The compound of claim 1, wherein R<sup>6</sup> is methyl or hydrogen

14. (Previously Presented) The compound of claim 1, wherein R<sup>6</sup> is methyl.

15. (Previously Presented) The compound of claim 1, wherein R<sup>6</sup> is hydrogen.

16. (Previously Presented) The compound of claim 1, wherein W is CH or N.

17. (Previously Presented) The compound of claim 1, wherein W is CH.

18. (Currently Amended) The compound of claim 1, wherein W is N.

19. (Previously Presented) The compound of claim 1, wherein V is  $-M-R^{10}$  or  $R^{14}$ .
20. (Previously Presented) The compound of claim 1, wherein M is  $-C(=O)NR^4$ .
21. (Previously Presented) The compound of claim 1, wherein M is  $-C(=O)NH-$ .
22. (Previously Presented) The compound of claim 1, wherein  $R^{10}$  is alkoxyalkyl.
23. (Previously Presented) The compound of claim 1, wherein  $R^{10}$  is methoxybenzyl.
24. (Previously Presented) The compound of claim 1, wherein  $R^{14}$  is aryl or heteroaryl optionally substituted with up to three  $R^{12}$ .
25. (Previously Presented) The compound of claim 1, wherein  $R^{14}$  is heteroaryl optionally substituted with lower alkyl.
26. (Previously Presented) The compound of claim 1, wherein  $R^{14}$  is oxadiazolyl, optionally substituted with methyl.
27. (Previously Presented) The compound of claim 1, wherein P is  $-C(=O)-R^{10}$  or  $R^{15}$ , where  $R^{10}$  is aryl and  $R^{15}$  is aryl or heteroaryl optionally substituted with up to three  $R^{12}$ .
28. (Previously Presented) The compound of claim 1, wherein  $R^1$  is selected from lower alkyl, lower cycloalkyl and halogen.
29. (Previously Presented) The compound of claim 1, wherein  $R^1$  is lower alkyl.
30. (Previously Presented) The compound of claim 1, wherein  $R^1$  is methyl.
31. (Previously Presented) The compound of claim 1, wherein  $R^2$  is selected from lower alkyl, lower cycloalkyl and halogen.

32. (Previously Presented) The compound of claim 1, wherein R<sup>2</sup> is hydrogen.
33. (Previously Presented) The compound of claim 1, wherein L is -CONH-.
34. (Previously Presented) The compound of claim 1, wherein R<sup>3</sup> is selected from lower alkyl, lower cycloalkyl, heteroaryl, substituted heteroaryl.
35. (Previously Presented) The compound of claim 1, wherein R<sup>3</sup> is lower cycloalkyl.
36. (Previously Presented) The compound of claim 1, wherein R<sup>3</sup> is cyclopropyl.
37. (Currently Amended) The compound of claim 1 selected from:  
 6-Methyl-4'-[1,3,4]oxadiazol-2-yl-biphenyl-3-carboxylic acid cyclopropylamide;  
 6-Methyl-4'-(5-methyl-[1,3,4]oxadiazol-2-yl)-biphenyl-3-carboxylic acid cyclopropylamide;  
 6-Methyl-4'-(4H-[1,2,4]triazol-3-yl)-biphenyl-3-carboxylic acid cyclopropylamide;  
~~N-Cyclopropyl 4-methyl 3-(5-[1,3,4]oxadiazol-2-yl-pyridin-2-yl)-benzamide;~~  
~~N-Cyclopropyl 4-methyl 3-[5-(5-methyl-[1,3,4]oxadiazol-2-yl)-pyridin-2-yl]-benzamide;~~  
~~3-(3-Benzyl-4-oxo-3,4-dihydro-quinazolin-7-yl)-N-cyclopropyl-4-methyl-benzamide;~~  
~~N-Cyclopropyl 3-[3-(2,6-dichloro-benzyl)-4-oxo-3,4-dihydro-quinazolin-7-yl]-4-methyl-benzamide;~~  
~~N-Cyclopropyl 3-[3-(3,4-dichloro-benzyl)-4-oxo-3,4-dihydro-quinazolin-7-yl]-4-methyl-benzamide;~~  
~~N-Cyclopropyl 3-[3-(4-methoxy-benzyl)-4-oxo-3,4-dihydro-quinazolin-7-yl]-4-methyl-benzamide;~~  
~~N-Cyclopropyl 4-methyl 3-(4-oxo-3,4-dihydro-quinazolin-7-yl)-benzamide;~~  
 4'-Benzoyl-6-methyl-biphenyl-3-carboxylic acid cyclopropylamide;  
~~6-(5-Cyclopropylcarbamoyl-2-methyl-phenyl)-N-(4-methoxy-benzyl)-nicotinamide;~~  
~~N-(4-Methoxybenzyl)-2-[(5-cyclopropylaminocarbonyl)-2-methylphenyl]-4-aminopyrimidine-5-carboxamide;~~  
 3'-Amino-4'-benzoyl-6-methyl-biphenyl-3-carboxylic acid cyclopropylamide;  
~~N-Cyclopropyl 4-methyl 3-(2-oxo-4-phenyl-1,2-dihydro-quinazolin-7-yl)-benzamide;~~  
~~N-Cyclopropyl 4-methyl 3-(4-phenyl-quinazolin-7-yl)-benzamide;~~ and  
 3'-Acetylamino-4'-benzoyl-6-methyl-biphenyl-3-carboxylic acid cyclopropylamide.

38. (Previously Presented) A method of treating, preventing, or ameliorating one or more symptoms of p38 kinase-mediated diseases or disorders, comprising administering to a subject in need thereof a compound of claim 1.

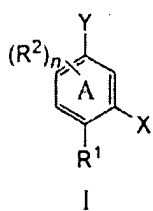
39. (Original) The method of claim 38, wherein the disease or disorder is selected from inflammatory diseases, autoimmune diseases, destructive bone disorders, proliferative disorders, angiogenic disorders, infectious diseases, neurodegenerative diseases, and viral diseases.

40. (Previously Presented) The method of claim 37, wherein the disease or disorder is selected from pancreatitis (acute or chronic), asthma, allergies, adult respiratory distress syndrome, chronic obstructive pulmonary disease, glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Grave's disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, graft vs. host disease, inflammatory reaction induced by endotoxin, tuberculosis, atherosclerosis, muscle degeneration, cachexia, psoriatic arthritis, Reiter's syndrome, gout, traumatic arthritis, rubella arthritis, acute synovitis, pancreatic  $\beta$ -cell disease; diseases characterized by massive neutrophil infiltration; rheumatoid spondylitis, gouty arthritis and other arthritic conditions, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcoisosis, bone resorption disease, allograft rejections, fever and myalgias due to infection, cachexia secondary to infection, meloid formation, scar tissue formation, ulcerative colitis, pyresis, influenza, osteoporosis, osteoarthritis and multiple myeloma-related bone disorder, acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma, sepsis, septic shock, and Shigellosis; Alzheimer's disease, Parkinson's disease, cerebral ischemias or neurodegenerative disease caused by traumatic injury; angiogenic disorders including solid tumors, ocular neovascularization, and infantile haemangiomas; viral diseases including acute hepatitis infection (including hepatitis A, hepatitis B and hepatitis C), HIV infection and CMV retinitis, AIDS, SARS, ARC or malignancy, and herpes; stroke, myocardial ischemia, ischemia in stroke heart attacks, organ hyposia, vascular hyperplasia, cardiac and renal reperfusion injury, thrombosis, cardiac hypertrophy, thrombin induced platelet aggregation, endotoxemia and/or toxic shock syndrome, and conditions associated with prostaglandin endoperoxidase synthase-2.

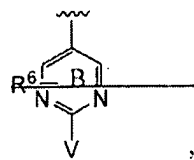
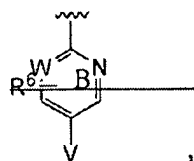
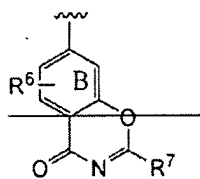
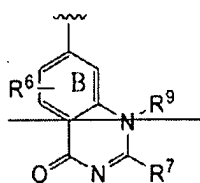
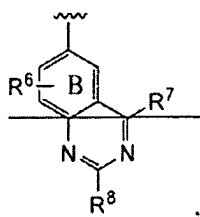
41. (Previously Presented) A method of inhibiting the expression of inducible pro-inflammatory proteins, comprising administering to a subject in need thereof a compound of claims 1.

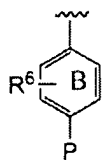
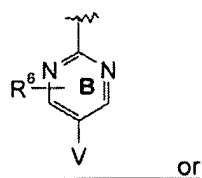
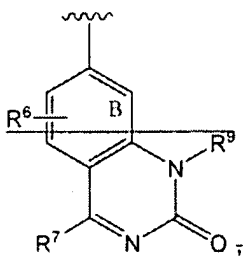
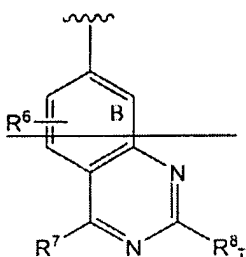
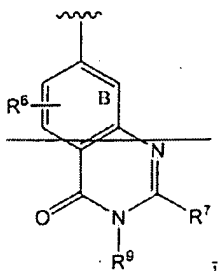
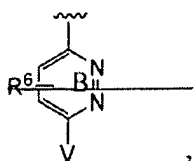
42. (Original) The method of claim 41, wherein the inducible pro-inflammatory protein is prostaglandin endoperoxide synthase-2 (PGHS-2), also referred to as cyclooxygenase-2 (COX-2).
43. (Previously Presented) A method of treating, preventing, or ameliorating one or more symptoms of diseases or disorders associated with inducible pro-inflammatory proteins, comprising administering to a subject in need thereof a compound of claim 1.
44. (Original) The method of claim 43, wherein the disease or disorder is selected from edema, analgesia, fever, pain, neuromuscular pain, headache, pain caused by cancer, dental pain and arthritis pain.
45. (Original) The method of claim 40, wherein the viral infection is a veterinary viral infection.
46. (Original) The method of claim 45, wherein the veterinary viral infection is lentivirus infection, equine infectious anemia virus; retro virus infection, feline immunodeficiency virus, bovine immunodeficiency virus, and canine immunodeficiency virus.
47. (Previously Presented) A method of treating, preventing, or ameliorating one or more symptoms of a cytokine mediated disease or disorder, comprising administering to a subject in need thereof a compound of claim 1.
48. (Previously Presented) The method of claims 38, further comprising administering a corticosteroid, rolipram, calphostin, a CSAID, a 4-substituted imidazo[1,2-A]quinoxaline, interleukin-10, a glucocorticoid, a salicylate, nitric oxide, an immunosuppressant, a nuclear translocation inhibitor, deoxyspergualin (DSG); a non-steroidal antiinflammatory drug (NSAID), ibuprofen, celecoxib, rofecoxib; a steroid, prednisone, dexamethasone; an antiviral agent, abacavir; an antiproliferative agent, methotrexate, leflunomide, FK506; a cytotoxic drug, azathioprine, cyclophosphamide, a TNF- $\alpha$  inhibitor, tenidap, an anti-TNF antibody, a soluble TNF receptor, and rapamycin, or derivatives thereof.
49. (Previously Presented) A method of inhibiting p38 kinases, comprising contacting a p38 kinase with a compound of claim 1.
50. (Original) The method of claim 49, wherein the p38 kinase is p38 $\alpha$  or p38 $\beta$  kinases.

51. (Previously Presented) A method of mediating cytokine response, comprising administering to a subject in need thereof an effective amount of a compound of claim 1.
52. (Original) The method of claim 51, wherein the cytokine response is induced by p38 kinase activity.
53. (Previously Presented) A method of inhibiting inflammatory response, comprising administering to a subject in need thereof an effective amount of a compound of claim 1.
54. (Previously Presented) A pharmaceutical composition, comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
55. (Original) The pharmaceutical composition of claim 54 that is formulated for single dosage administration.
56. (Previously Presented) The pharmaceutical composition of claim 54, further comprising one or more of the following: corticosteroid, rolipram, calphostin, a CSAID, a 4-substituted imidazo[1,2-A]quinoxaline, interleukin-10, a glucocorticoid, a salicylate, nitric oxide, an immunosuppressant, a nuclear translocation inhibitor, deoxyspergualin (DSG); a non-steroidal antiinflammatory drug (NSAID), ibuprofen, celecoxib, rofecoxib; a steroid, prednisone, dexamethasone; an antiviral agent, abacavir; an antiproliferative agent, methotrexate, leflunomide, FK506; a cytotoxic drug, azathioprine, cyclophosphamide, a TNF- $\alpha$  inhibitor, tenidap, an anti-TNF antibody, a soluble TNF receptor, and rapamycin, or derivatives thereof.
57. (Previously Presented) An article of manufacture, comprising packaging material, a compound of claim 1 which is useful for treating, preventing, or ameliorating one or more symptoms of p38 kinase-mediated diseases or disorders, and a label that indicates that the compound is useful for treating, preventing, or ameliorating one or more symptoms of p38 kinase-mediated diseases or disorders.
58. (Currently Amended) A method of treating, preventing, or ameliorating one or more symptoms of p38 kinase-mediated diseases or disorders, comprising administering to a subject in need thereof a compound of formula (I):



or a pharmaceutically acceptable derivative thereof, wherein X is





$R^1$  is selected from hydrogen, halogen, hydroxyl, lower alkyl, lower cycloalkyl, alkynyl, trifluoromethyl, methoxy, trifluoromethoxy, cyano,  $-NH_2$ ,  $-NR^4R^5$  and  $-OR^4$ ;

$R^2$  is attached to any available carbon atom of the phenyl ring A and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy,  $-OMe$ ,  $-CN$ ,  $-NMe_2$ ,  $-S(=O)alkyl$ ,  $-S(=O)aryl$ ,  $-NHSO_2-aryl$ ,  $R^4$ ,  $-NHSO_2alkyl$ ,  $-CO_2R^4$ ,  $-CONH_2$ ,  $-SO_3H$ ,  $-S(O)alkyl$ ,  $-S(O)aryl$ ,  $-SO_2NHR^4$ , and  $-NHC(=O)NHR^4$ ;

$n$  is 0 or 1;

Y is  $-L-R^3$  or  $R^{11}$ ;

$R^3$  is selected from hydrogen, alkyl,  $-OR^4$ , substituted alkyl, cycloalkyl,  $-CR^4$ cycloalkyl, heteroaryl, substituted heteroaryl, heterocycle and substituted heterocycle;

L is  $-C(=O)NH-$ ,  $-NH(C=O)-$ ,  $-SO_2NH-$ ,  $-NHSO_2-$ , or  $-C(=O)-$ ;

$R^{11}$  is an optionally substituted 5-membered heteroaryl;

~~W is CH or N;~~

V is  $-M-R^{10}$  or  $R^{14}$ ;

M is  $-C(=O)NR^4-$ ,  $-NR^4(C=O)-$ ,  $-NR^4(C=O)NR^4-$ ,  $-NR^4SO_2-$ , or  $-C(=O)-$ ;

$R^{14}$  is aryl or heteroaryl optionally substituted with up to three  $R^{12}$ ;

P is  $-Q-R^{10}$  or  $R^{15}$ ;

Q is  $-NR^4(C=O)-$ ,  $-NR^4(C=O)NR^4-$ ,  $-SO_2NR^4-$ ,  $-NR^4SO_2-$ , or  $-C(=O)-$ ;

$R^{15}$  is aryl or heteroaryl optionally substituted with up to three  $R^{12}$ ;

$R^4$  and  $R^5$  are each selected independently from hydrogen, lower alkyl and lower cycloalkyl;

$R^6$  is attached to any available carbon atom of the phenyl ring B and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy,  $-OMe$ ,  $-CN$ ,  $-NH_2$ ,  $-NMe_2$ ,  $-S(=O)alkyl$ ,  $-S(=O)aryl$ ,  $-NHSO_2-aryl-R^4$ ,  $-NHSO_2alkyl$ ,  $-CO_2R^4$ ,  $-CONH_2$ ,  $-SO_3H$ ,  $-S(O)alkyl$ ,  $-S(O)aryl$ ,  $-SO_2NHR^4$ ,  $-NHC(=O)R^4$ , and  $-NHC(=O)NHR^4$ ;

~~$R^7$  and  $R^8$  are each independently selected from hydrogen, alkyl, substituted alkyl, aryl, and cycloalkyl;~~

~~$R^9$  is hydrogen, alkyl, substituted alkyl or cycloalkyl;~~

$R^{10}$  is alkyl, substituted alkyl, aryl, or  $-(CH_2)_tD-(CH_2)_e-R^{13}$ ;

t is selected from 0, 1, 2 and 3; e is selected from 0, 1, 2 and 3;

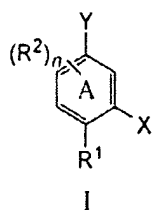
D is selected from a bond, an optionally substituted heterocycle, an optionally substituted aryl,  $-O-$ ,  $-S-$ ,  $-C(=O)-$ ,  $-NR^4(C=O)-$ ,  $-C(=O)NR^4-$ ,  $-S(O)-$ ,  $SO_2NR^4-$ ,  $SO_2-$ , and  $-NR^4-$ ;

$R^{12}$  is selected from  $R^{10}$ ,  $NO_2$ ,  $CN$ , lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy,  $-OMe$ ,  $-CN$ ,  $-NMe_2$ ,  $-S(=O)alkyl$ ,  $-S(=O)aryl$ ,  $-NHSO_2-aryl-R^4$ ,  $-NHSO_2alkyl$ ,  $-CO_2R^4$ ,  $-CONH_2$ ,  $-SO_3H$ ,  $-S(O)alkyl$ ,  $-S(O)aryl$ ,  $-SO_2NHR^4$ , and  $-NHC(=O)NHR^4$ ; and

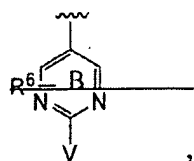
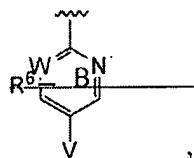
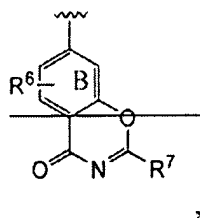
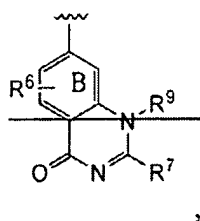
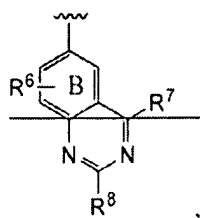
$R^{13}$  is selected from an optionally substituted five- to seven-membered heterocyclic ring, an optionally substituted five- to seven-membered heteroaryl ring and an optionally substituted fused bicyclic ring,

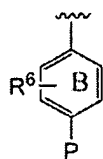
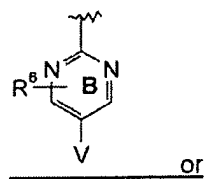
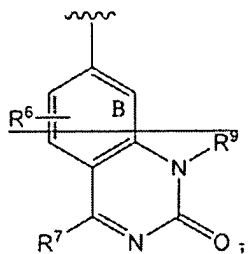
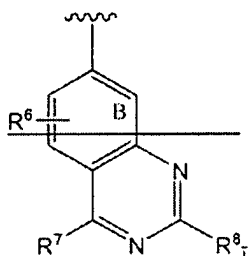
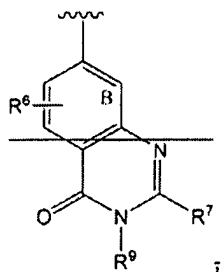
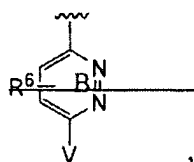
with the proviso that when Q is CO then Y is not oxadiazolyl and L is not  $-C(=O)NH-$  or  $-NHC(=O)-$ .

59. (Currently Amended) A method of inhibiting the expression of inducible pro-inflammatory proteins, comprising administering to a subject in need thereof a compound of formula (I):



or a pharmaceutically acceptable derivative thereof, wherein X is





R<sup>1</sup> is selected from hydrogen, halogen, hydroxyl, lower alkyl, lower cycloalkyl, alkynyl, trifluoromethyl, methoxy, trifluoromethoxy, cyano, -NH<sub>2</sub>, -NR<sup>4</sup>R<sup>5</sup> and -OR<sup>4</sup>;

R<sup>2</sup> is attached to any available carbon atom of the phenyl ring A and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo,

trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NMe<sub>2</sub>; -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>;

n is 0 or 1;

Y is -L-R<sup>3</sup> or R<sup>11</sup>;

R<sup>3</sup> is selected from hydrogen, alkyl, -OR<sup>4</sup>, substituted alkyl, cycloalkyl, -CR<sup>4</sup>cycloalkyl, heteroaryl, substituted heteroaryl, heterocycle and substituted heterocycle;

L is -C(=O)NH-, -NH(C=O)-, -SO<sub>2</sub>NH-, -NHSO<sub>2</sub>-, or -C(=O)-;

R<sup>11</sup> is an optionally substituted 5-membered heteroaryl;

~~W is CH or N;~~

V is -M-R<sup>10</sup> or R<sup>14</sup>;

M is -C(=O)NR<sup>4</sup>-, -NR<sup>4</sup>(C=O)-, -NR<sup>4</sup>(C=O)NR<sup>4</sup>-, -NR<sup>4</sup>SO<sub>2</sub>-, or -C(=O)-;

R<sup>14</sup> is aryl or heteroaryl optionally substituted with up to three R<sup>12</sup>;

P is -Q-R<sup>10</sup> or R<sup>15</sup>;

Q is -NR<sup>4</sup>(C=O)-, -NR<sup>4</sup>(C=O)NR<sup>4</sup>-, -SO<sub>2</sub>NR<sup>4</sup>-, -NR<sup>4</sup>SO<sub>2</sub>-, or -C(=O)-;

R<sup>15</sup> is aryl or heteroaryl optionally substituted with up to three R<sup>12</sup>;

R<sup>4</sup> and R<sup>5</sup> are each selected independently from hydrogen, lower alkyl and lower cycloalkyl;

R<sup>6</sup> is attached to any available carbon atom of the phenyl ring B and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NH<sub>2</sub>, -NMe<sub>2</sub>; -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, -NHC(=O)R<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>;

~~R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen, alkyl, substituted alkyl, aryl, and cycloalkyl;~~

~~R<sup>9</sup> is hydrogen, alkyl, substituted alkyl or cycloalkyl;~~

R<sup>10</sup> is alkyl, substituted alkyl, aryl, or -(CH<sub>2</sub>)<sub>t</sub>-D-(CH<sub>2</sub>)<sub>e</sub>-R<sup>13</sup>;

t is selected from 0, 1, 2 and 3; e is selected from 0, 1, 2 and 3;

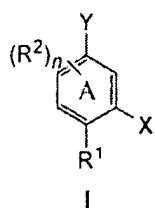
D is selected from a bond, an optionally substituted heterocycle, an optionally substituted aryl, -O-, -S-, -C(=O)-, -NR<sup>4</sup>(C=O)-, -C(=O)NR<sup>4</sup>-, -S(O)-, SO<sub>2</sub>NR<sup>4</sup>-, SO<sub>2</sub>-, and -NR<sup>4</sup>-;

R<sup>12</sup> is selected from R<sup>10</sup>, NO<sub>2</sub>, CN, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NMe<sub>2</sub>; -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>; and

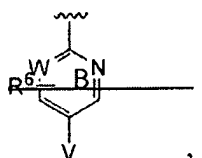
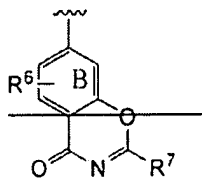
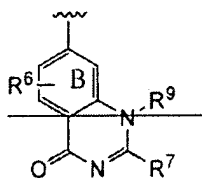
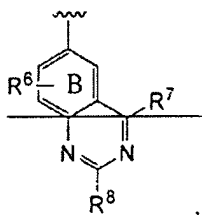
$R^{13}$  is selected from an optionally substituted five- to seven-membered heterocyclic ring, an optionally substituted five- to seven-membered heteroaryl ring and an optionally substituted fused bicyclic ring,

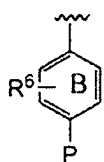
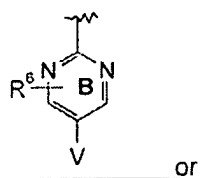
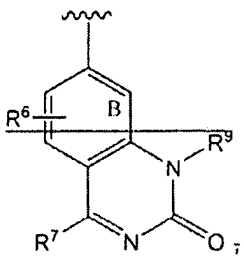
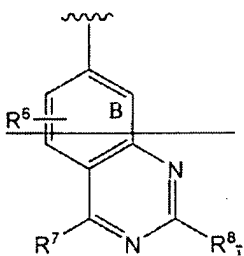
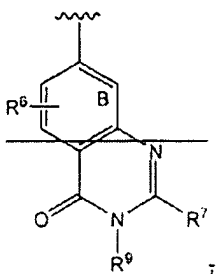
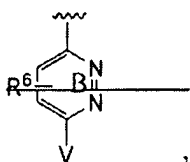
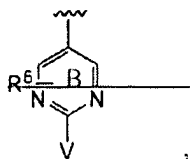
with the proviso that when Q is CO then Y is not oxadiazolyl and L is not  $-C(=O)NH-$  or  $-NHC(=O)-$ .

60. (Currently Amended) A method of treating, preventing, or ameliorating one or more symptoms of diseases or disorders associated with inducible pro-inflammatory proteins, comprising administering to a subject in need thereof a compound of formula (I):



or a pharmaceutically acceptable derivative thereof, wherein X is





;

R<sup>1</sup> is selected from hydrogen, halogen, hydroxyl, lower alkyl, lower cycloalkyl, alkynyl, trifluoromethyl, methoxy, trifluoromethoxy, cyano, -NH<sub>2</sub>, -NR<sup>4</sup>R<sup>5</sup> and -OR<sup>4</sup>;

R<sup>2</sup> is attached to any available carbon atom of the phenyl ring A and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NMe<sub>2</sub>, -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>;

n is 0 or 1;

Y is -L-R<sup>3</sup> or R<sup>11</sup>;

R<sup>3</sup> is selected from hydrogen, alkyl, -OR<sup>4</sup>, substituted alkyl, cycloalkyl, -CR<sup>4</sup>cycloalkyl, heteroaryl, substituted heteroaryl, heterocycle and substituted heterocycle;

L is -C(=O)NH-, -NH(C=O)-, -SO<sub>2</sub>NH-, -NHSO<sub>2</sub>-, or -C(=O)-;

R<sup>11</sup> is an optionally substituted 5-membered heteroaryl;

~~W is CH or N;~~

V is -M-R<sup>10</sup> or R<sup>14</sup>;

M is -C(=O)NR<sup>4</sup>-, -NR<sup>4</sup>(C=O)-, -NR<sup>4</sup>(C=O)NR<sup>4</sup>-, -NR<sup>4</sup>SO<sub>2</sub>-, or -C(=O)-;

R<sup>14</sup> is aryl or heteroaryl optionally substituted with up to three R<sup>12</sup>;

P is -Q-R<sup>10</sup> or R<sup>15</sup>;

Q is -NR<sup>4</sup>(C=O)-, -NR<sup>4</sup>(C=O)NR<sup>4</sup>-, -SO<sub>2</sub>NR<sup>4</sup>-, -NR<sup>4</sup>SO<sub>2</sub>-, or -C(=O)-;

R<sup>15</sup> is aryl or heteroaryl optionally substituted with up to three R<sup>12</sup>;

R<sup>4</sup> and R<sup>5</sup> are each selected independently from hydrogen, lower alkyl and lower cycloalkyl;

R<sup>6</sup> is attached to any available carbon atom of the phenyl ring B and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NH<sub>2</sub>, -NMe<sub>2</sub>, -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, -NHC(=O)R<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>;

~~R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen, alkyl, substituted alkyl, aryl, and cycloalkyl;~~

~~R<sup>9</sup> is hydrogen, alkyl, substituted alkyl or cycloalkyl;~~

R<sup>10</sup> is alkyl, substituted alkyl, aryl, or -(CH<sub>2</sub>)<sub>t</sub>-D-(CH<sub>2</sub>)<sub>e</sub>-R<sup>13</sup>;

t is selected from 0, 1, 2 and 3; e is selected from 0, 1, 2 and 3;

D is selected from a bond, an optionally substituted heterocycle, an optionally substituted aryl, -O-, -S-, -C(=O)-, -NR<sup>4</sup>(C=O)-, -C(=O)NR<sup>4</sup>-, -S(O)-, SO<sub>2</sub>NR<sup>4</sup>-, SO<sub>2</sub>-, and -NR<sup>4</sup>-;

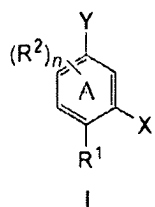
R<sup>12</sup> is selected from R<sup>10</sup>, NO<sub>2</sub>, CN, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NMe<sub>2</sub>, -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -

NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>; and

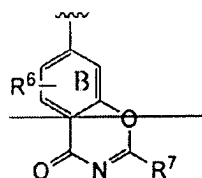
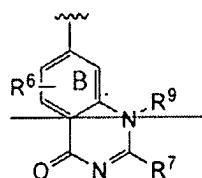
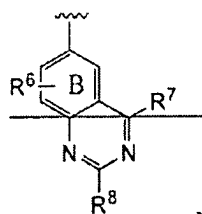
R<sup>13</sup> is selected from an optionally substituted five- to seven-membered heterocyclic ring, an optionally substituted five- to seven-membered heteroaryl ring and an optionally substituted fused bicyclic ring,

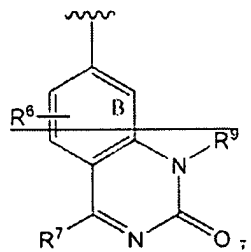
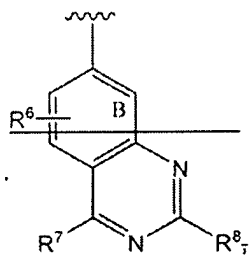
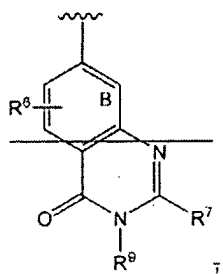
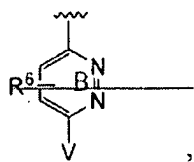
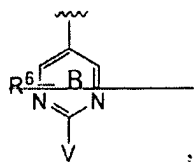
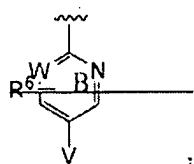
with the proviso that when Q is CO then Y is not oxadiazolyl and L is not -C(=O)NH- or -NHC(=O).

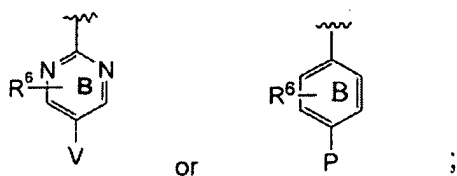
61. (Currently Amended) A method of mediating cytokine response comprising administering to a subject in need thereof a compound of formula (I):



or a pharmaceutically acceptable derivative thereof, wherein X is







$R^1$  is selected from hydrogen, halogen, hydroxyl, lower alkyl, lower cycloalkyl, alkynyl, trifluoromethyl, methoxy, trifluoromethoxy, cyano,  $-NH_2$ ,  $-NR^4R^5$  and  $-OR^4$ ;

$R^2$  is attached to any available carbon atom of the phenyl ring A and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy,  $-OMe$ ,  $-CN$ ,  $-NMe_2$ ,  $-S(=O)alkyl$ ,  $-S(=O)aryl$ ,  $-NHSO_2-aryl-R^4$ ,  $-NHSO_2alkyl$ ,  $-CO_2R^4$ ,  $-CONH_2$ ,  $-SO_3H$ ,  $-S(O)alkyl$ ,  $-S(O)aryl$ ,  $-SO_2NHR^4$ , and  $-NHC(=O)NHR^4$ ;

$n$  is 0 or 1;

$Y$  is  $-L-R^3$  or  $R^{11}$ ;

$R^3$  is selected from hydrogen, alkyl,  $-OR^4$ , substituted alkyl, cycloalkyl,  $-CR^4cycloalkyl$ , heteroaryl, substituted heteroaryl, heterocycle and substituted heterocycle;

$L$  is  $-C(=O)NH-$ ,  $-NH(C=O)-$ ,  $-SO_2NH-$ ,  $-NHSO_2-$  or  $-C(=O)-$ ;

$R^{11}$  is an optionally substituted 5-membered heteroaryl;

~~W is CH or N;~~

$V$  is  $-M-R^{10}$  or  $R^{14}$ ;

$M$  is  $-C(=O)NR^4-$ ,  $-NR^4(C=O)-$ ,  $-NR^4(C=O)NR^4-$ ,  $-NR^4SO_2-$ , or  $-C(=O)-$ ;

$R^{14}$  is aryl or heteroaryl optionally substituted with up to three  $R^{12}$ ;

$P$  is  $-Q-R^{10}$  or  $R^{15}$ ;

$Q$  is  $-NR^4(C=O)-$ ,  $-NR^4(C=O)NR^4-$ ,  $-SO_2NR^4-$ ,  $-NR^4SO_2-$ , or  $-C(=O)-$ ;

$R^{15}$  is aryl or heteroaryl optionally substituted with up to three  $R^{12}$ ;

$R^4$  and  $R^5$  are each selected independently from hydrogen, lower alkyl and lower cycloalkyl;

$R^6$  is attached to any available carbon atom of the phenyl ring B and at each occurrence is independently selected from hydrogen, alkyl, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy,  $-OMe$ ,  $-CN$ ,  $-NH_2$ ,  $-NMe_2$ ,  $-S(=O)alkyl$ ,  $-S(=O)aryl$ ,  $-NHSO_2-aryl-R^4$ ,  $-NHSO_2alkyl$ ,  $-CO_2R^4$ ,  $-CONH_2$ ,  $-SO_3H$ ,  $-S(O)alkyl$ ,  $-S(O)aryl$ ,  $-SO_2NHR^4$ ,  $-NHC(=O)R^4$ , and  $-NHC(=O)NHR^4$ ;

~~$R^7$  and  $R^8$  are each independently selected from hydrogen, alkyl, substituted alkyl, aryl, and cycloalkyl;~~

~~$R^9$  is hydrogen, alkyl, substituted alkyl or cycloalkyl;~~

$R^{10}$  is alkyl, substituted alkyl, aryl, or  $-(CH_2)_t-D-(CH_2)_e-R^{13}$ ;

$t$  is selected from 0, 1, 2 and 3;  $e$  is selected from 0, 1, 2 and 3;

D is selected from a bond, an optionally substituted heterocycle, an optionally substituted aryl, -O-, -S-, -(C=O)-, -NR<sup>4</sup>(C=O)-, -(C=O)NR<sup>4</sup>-, -S(O)-, SO<sub>2</sub>NR<sup>4</sup>-, SO<sub>2</sub>-, and -NR<sup>4</sup>-;

R<sup>12</sup> is selected from R<sup>10</sup>, NO<sub>2</sub>, CN, lower cycloalkyl, halo, trifluoromethyl, trifluoromethoxy, -OMe, -CN, -NMe<sub>2</sub>, -S(=O)alkyl, -S(=O)aryl, -NHSO<sub>2</sub>-aryl-R<sup>4</sup>, -NHSO<sub>2</sub>alkyl, -CO<sub>2</sub>R<sup>4</sup>, -CONH<sub>2</sub>, -SO<sub>3</sub>H, -S(O)alkyl, -S(O)aryl, -SO<sub>2</sub>NHR<sup>4</sup>, and -NHC(=O)NHR<sup>4</sup>; and

R<sup>13</sup> is selected from an optionally substituted five- to seven-membered heterocyclic ring, an optionally substituted five- to seven-membered heteroaryl ring and an optionally substituted fused bicyclic ring,

with the proviso that when Q is CO then Y is not oxadiazolyl and L is not -C(=O)NH- or -NHC(=O).